UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,145	05/05/2005	Charles Reay MacKay	RICE-032	8992

24353 7590 04/04/2008

BOZICEVIC, FIELD & FRANCIS LLP
1900 UNIVERSITY AVENUE
SUITE 200
EAST PALO ALTO, CA 94303

EXAMINER	
VANDERVEGT, FRANCOIS P	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
04/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/502,145	MACKAY, CHARLES REAY	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-51* is/are pending in the application.

4a) Of the above claim(s) *40-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-26,29-32 and 36-39* is/are rejected.

7)☒ Claim(s) *2,27,28 and 33-35* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :20041015, 20041115, 20041202, 20051115.

DETAILED ACTION

This application is a Rule 371 continuation of PCT Serial Number PCT/AU03/00084, which claims the benefit of the filing date of provisional U.S. Application 60/350,961.

Claims 1-51 are currently pending.

Election/Restrictions

1. Applicant's suggestion regarding further restriction of Group I is acknowledged. Upon further review, Applicant's suggestion is accepted. Accordingly, the Groups now comprise the following claim numbers:

Group I - claims 1-39 (as altered)

Group II - claims 43-46

Group III - claims 49, 50

Group IV - claim 51

Group V - claims 40-42, 47 and 48 (as altered)

Applicant's election without traverse of Group I, claims 1-39, in the reply filed on January 3, 2008 is acknowledged.

Claims 40-51 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on January 3, 2008.

Accordingly, **claims 1-39 are the subject of examination** in the present Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 3-8 and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The hybridoma cell lines deposited with ECACC under accession numbers 00110609,

02090226 and 02090227 producing the antibodies 7F3, 6C12 and 12D4 are required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of *35 U.S.C. 112*, first paragraph, may be satisfied by a deposit of said cell lines. *See 37 C.F.R. 1.802.*

It is noted that the deposits have been made under the terms of the Budapest Treaty. However, in addition an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the hybridomas will be **irrevocably** and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample **or for the enforceable life of the patent**, whichever is longer. See 37 CFR 1.806.

Additionally, amendment of the specification to disclose the date of deposit and the complete name and current address of the depository is required.

Applicant's attention is directed to *In re Lundak*, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985), and 37 CFR 1.801-1.809 for further information concerning deposit practice.

3. Claims 10-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody comprising all six of the CDR regions of an antibody produced by one of the hybridomas disclosed as 00110609, 02090226 and 02090227, does not reasonably provide enablement for the broad recitation of an antibody comprising only one or two of the individual CDR regions of an antibody or of only the heavy or light chain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

It is well established in the art that the formation of an intact antigen-binding site

generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity that is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff (Proc Natl Acad Sci USA [1982] 79:1979-1983; U on form PTO-892). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function (see entire document).

MacCallum (J. Mol. Biol. [1996] 262:732-745; V on form PTO-892) analyzed a number of different antibodies for interactions with antigen and discloses that the CDR3s of the heavy and light chain dominate, however a number of residues outside the standard CDR definitions make antigen contacts (page 733, column 2 in particular) and non-contacting residues within the CDRs coincide with residues as important in defining canonical backbone conformations (page 735, column 1 in particular).

Casset (Biochem. Biophys. Res. Comm. [2003] 307:198-205; W on form PTO-892) underscores the fact that not just one CDR is essential for antigen binding or maintaining the conformation of the antigen-binding site as shown in the case of the construction of a peptide mimetic of an anti-CD4 monoclonal antibody binding site by rational design. The peptide was designed with 27 residues formed by residues from 5 CDRs (see entire document). Casset discloses that although CDR H3 is at the center of most if not all antigen interactions, clearly other CDRs play an important role in the recognition process (page 199, column 1 in particular) and this is demonstrated in this work by using all CDRs except L2 and additionally using a framework residue located just before the H3 (page 202, column 1 in particular).

Wu (J. Mol. Biol. [1999] 294:151-162; X on form PTO-892) discloses that it is difficult to predict which framework residues serve a critical role in maintaining affinity and specificity due in part to the large conformational change in antibodies that accompany antigen binding but certain residues have been identified as important for maintaining conformation (page 152,

column 1 in particular).

Accordingly, in view of the limited guidance provided by the specification, the level of predictability in the art, the nature of the claimed invention and the undue experimentation required of one of ordinary skill in the art, it would require an undue amount of trial and error to practice the full scope of the invention and this is not sanctioned by the statute.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 3-8 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is indefinite and ambiguous to recite the laboratory names 7F3, 6C12 and 12D4 in claims 3-8 and 29 to identify the antibodies. The same designations may likely to be used by others as well to designate different antibodies or cell lines. It is suggested that the corresponding accession or deposit numbers from an acceptable depository be recited in the claim.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 9, 25, 26, and 36-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Farkas et al (Neuroreport [1999] 10:3021-3025; cited on form PTO-1449 filed 10/15/04).

Farkas et al teaches 4C8, a monoclonal IgM antibody that is reactive with amino acid residues 101-116, the first extracellular loop, of C5a receptor (page 3022, first column in particular). Farkas also teaches the detection of 4C8 with fluorescent labeled goat anti-mouse antibody, satisfying the metes and bounds of a conjugate comprising a detectable label [claims 36, 37] (page 3022 in particular). Farkas teaches that the antibodies are diluted in Hanks' balanced salt solution, which comprises water,, a pharmaceutically acceptable carrier [claim 39] (page 3022, second column in particular). Claim 9 is included because the method used to

determine the antibody's ability to bind to C5aR does not affect the binding properties of the antibody. Claim 25 is included because, while Farkas is silent about the ability of the antibody to inhibit neutrophil attraction by means other than C5a, silence about a particular property does not necessarily constitute the absence of that property. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that there is a difference between the materials, i.e., that the claims are directed to new materials and that such a difference would have been considered unexpected by one of ordinary skill in the art, that is, the claimed subject matter, if new, is unobvious. In the absence of evidence to the contrary, the burden is on the Applicant to prove that the claimed materials are different from t those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989). The prior art teaching anticipates the claimed invention. Claim 38 is included because it would be well within the purview of the artisan to isolate the nucleic acid encoding the antibody.

Conclusion

6. Claims 2, 27, 28 and 33-35 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571)272-0852. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571) 272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

F. Pierre VanderVegt, Ph.D. /PV/
Patent Examiner
March 29, 2008

/David A Saunders/
Primary Examiner, Art Unit 1644